

Amendments to the Specification

Please replace the paragraph on page 1 that begins on line 3 with the following amended paragraph:

This application is a continuation of U.S. Application No. 09/438,538, filed November 12, 1999 (now abandoned), which is a division of U.S. Application No. 09/042,105, filed March 13, 1998 (now U.S. Patent No. 6,040,157, issued on March 21, 2000), which is a continuation-in-part of U.S. Application No. 08/999,811, filed December 24, 1997 (now issued U.S. Patent No. 5,932,540), which is a continuation-in-part of both U.S. ~~Applications~~ Serial Application No. 08/465,968, filed June 6, 1995 (now issued U.S. Patent No. 6,608,182), and ~~Serial~~ U.S. Application No. 08/207,550, (now abandoned), said 08/465,968 is a continuation-in-part of U.S. Application ~~Serial~~ No. 08/207,550, filed March 8, 1994 (now abandoned), all of which claim priority under 35 U.S.C. § 120, and all are hereby incorporated by reference in their entirety.

Please replace the paragraph on page 8 that begins on line 19 with the following amended paragraph:

FIGs. ~~26 A-G depicts~~ 26A-26G depict the ability of VEGF2 to affect the diastolic blood pressure in spontaneously hypertensive rats (SHR). FIGs. 26a and b depict the dose-dependent decrease in diastolic blood pressure achieved with VEGF2. (FIGs. 26c and d depict the decreased mean arterial pressure (MAP) observed with VEGF2. For

FIGs. 26E-G, increasing doses of VEGF-2 (HG00403-B8, HG00404-C5, and HG00404-C4) were administered to 13-14 week old SHR and the data are expressed as the mean +/- SEM. Statistical analysis were performed with a paired t-test and significance was defined as $p < 0.05$ vs. the response buffer alone. Panel E shows the effect of increasing doses of VEGF-2 on the mean arterial pressure (MAP) of SHR rats. The response to B8 and C4 were significant at the 300 $\mu\text{g/kg}$ dose. The response to C5 was significant at the 100, 300 and 900 $\mu\text{g/kg}$ doses. Panel F shows the effect of VEGF-2 on the diastolic blood pressure of SHR rats. The response to B8 was significant at the 300 $\mu\text{g/kg}$ dose. Administration of C5 yielded significant responses at doses greater than or equal to 100 $\mu\text{g/kg}$. The response to C4 was significant when 10, 100, 300 and 900 $\mu\text{g/kg}$ were given. Panel G shows the effect of VEGF-2 on the diastolic blood pressure of SHR rats. The response to B8 was significant only at the 300 $\mu\text{g/kg}$ dose and when given acetylcholine. The responses to C4 and C5, while much less dramatic, were statistically significant at all dose levels.

Please replace the paragraph on page 9 that begins on line 8 with the following amended paragraph:

In accordance with one aspect of the present invention, there are provided isolated nucleic acid molecules comprising a polynucleotide encoding a VEGF2 polypeptide having the deduced amino acid sequence of Figure 1 (SEQ ID NO:2), which was determined by sequencing a cloned cDNA. The nucleotide sequence shown in SEQ ID NO:1 was obtained by sequencing a cDNA clone, which was deposited on May 12,

1995 at the ~~American Type Tissue Collection (ATCC), 12301 Park Lawn Drive, Rockville, Maryland 20852,~~ American Type Culture Collection (ATCC), Patent Depository, 10801 University Boulevard, Manassas, VA 20110, and given ATCC Deposit No. 97149.

Please replace the paragraph on page 9 that begins on line 16 with the following amended paragraph:

In accordance with another aspect of the present invention, there are provided isolated nucleic acid molecules comprising a polynucleotide encoding a truncated VEGF2 polypeptide having the deduced amino acid sequence of Figure 2 (SEQ ID NO:4), which was determined by sequencing a cloned cDNA. The nucleotide sequence shown in SEQ ID NO:3 was obtained by sequencing a cDNA clone, which was deposited on March 4, 1994 at the ~~American Type Tissue Collection (ATCC), 12301 Park Lawn Drive, Rockville, Maryland 20852,~~ American Type Culture Collection (ATCC), Patent Depository, 10801 University Boulevard, Manassas, VA 20110, and given ATCC Deposit Number 75698.

Please replace the paragraph beginning at page 22, line 6 with the following amended paragraph:

Particularly preferred VEGF-2 polypeptides are shown below (numbering starts with the first amino acid in the protein (Met) (Figure 1 (SEQ ID NO:18)):

Ala (residue <u>24 25</u>) -- Ser (residue 419)	Glu (<u>32 33</u>) -- Ser (419)
Pro (<u>25 26</u>) -- Ser (419)	Ser (<u>33 34</u>) -- Ser (419)
Ala (<u>26 27</u>) -- Ser (419)	Gly (<u>34 35</u>) -- Ser (419)
Ala (<u>27 28</u>) -- Ser (419)	Leu (<u>35 36</u>) -- Ser (419)
Ala (<u>28 29</u>) -- Ser (419)	Asp (<u>36 37</u>) -- Ser (419)
Ala (<u>29 30</u>) -- Ser (419)	Leu (<u>37 38</u>) -- (Ser (419))
Ala (<u>30 31</u>) -- Ser (419)	Ser (<u>38 39</u>) -- Ser (419)
Phe (<u>31 32</u>) -- Ser (419)	Asp (<u>39 40</u>) -- Ser (419)
	Ala (<u>40 41</u>) -- Ser (419)
Glu (<u>41 42</u>) -- Ser (419)	Met(1), Glu (<u>23 24</u>), or Ala (<u>24 25</u>) -- Gln (414)
Pro (<u>42 43</u>) -- Ser (419)	Met(1), Glu (<u>23 24</u>), or Ala (<u>24 25</u>) -- Trp (413)
Asp (<u>43 44</u>) -- Ser (419)	Met(1), Glu (<u>23 24</u>), or Ala (<u>24 25</u>) -- Tyr (412)
Ala ([[44]] <u>45</u>) -- Ser (419)	Met(1), Glu (<u>23 24</u>), or Ala (<u>24 25</u>) -- Ser (411)
Gly (<u>45 46</u>) -- Ser (419)	Met(1), Glu (<u>23 24</u>), or Ala (<u>24 25</u>) -- Pro (410)
Glu (<u>46 47</u>) -- Ser (419)	Met(1), Glu (<u>23 24</u>), or Ala (<u>24 25</u>) -- Val (409)
Ala (<u>47 48</u>) -- Ser (419)	Met (1), Glu (<u>23 24</u>), or Ala (<u>24 25</u>) -- Cys (408)
Thr (<u>48 49</u>) -- Ser (419)	Met (1), Glu (<u>23 24</u>), or Ala (<u>24 25</u>) -- Arg (407)
Ala (<u>49 50</u>) -- Ser (419)	Met(1), Glu (<u>23 24</u>), or Ala (<u>24 25</u>) -- Cys (406)
Tyr (<u>50 51</u>) -- Ser (419)	Met(1), Glu (<u>23 24</u>), or Ala (<u>24 25</u>) -- Val (405)
Ser (<u>52 53</u>) -- Ser (419)	Met(1), Gly (<u>23 24</u>), or Ala (<u>24 25</u>) -- Glu (404)
Asp (<u>54 55</u>) -- Ser (419)	Met(1), Glu (<u>23 24</u>), or Ala (<u>24 25</u>) -- Glu (403)
Val (<u>62 63</u>) -- Ser (419)	Met(1), Glu (<u>23 24</u>), or Ala (<u>24 25</u>) -- Ser (402)
Val (<u>65 66</u>) -- Ser (419)	Met(1), Glu (<u>23 24</u>), or Ala (<u>24 25</u>) -- Gly (398)
Met(1), Glu (<u>23 24</u>), or Ala (<u>24 25</u>) -- Met (418)	Met(1), Glu (<u>23 24</u>), or Ala (<u>24 25</u>) -- Pro (397)
Met(1), Glu (<u>23 24</u>), or Ala (<u>24 25</u>) -- Gln (417)	Met(1), Glu (<u>23 24</u>), or Ala (<u>24 25</u>) -- Lys (393)
Met(1), Glu (<u>23 24</u>), or Ala (<u>24 25</u>) -- Pro (416)	Met(1), Glu (<u>23 24</u>), or Ala (<u>24 25</u>) -- Met(263)
Met(1), Glu (<u>23 24</u>), or Ala (<u>24 25</u>) -- Arg (415)	

Met(1), Glu (23 <u>24</u>), or Ala (24 <u>25</u>) -- Asp(311)	Tyr(114) -- Ser(228)
Met(1), Glu (23 <u>24</u>), or Ala (24 <u>25</u>) -- Pro (367 <u>366</u>)	Asn(115) -- Ser(228)
Met(1) -- Ser (419)	Thr(116) -- Ser(228)
Met(1) -- Ser(228)	Thr(103) -- Leu(229)
Glu(47) -- Ser(419)	Glu(104) -- Leu(229)
Ala(111) -- Lys(214)	Thr(103) -- Arg(227)
Ala(112) -- Lys(214)	Glu(104) -- Arg(227)
His(113) -- Lys(214)	Glu(105) -- Arg(227)
Tyr(114) -- Lys(214)	Thr(106) -- Arg(227)
Asn(115) -- Lys(214)	Ile(107) -- Arg(227)
Thr(116) -- Lys(214)	Lys(108) -- Arg(227)
Thr(103) -- Leu(215)	Phe(109) -- Arg(227)
Glu(104) -- Leu(215)	Ala(110) -- Arg(227)
Glu(105) -- Leu(215)	Ala(111) -- Arg(227)
Thr(106) -- Leu(215)	Ala(112) -- Arg(227)
Ile(107) -- Leu(215)	His(113) -- Arg(227)
Lys(108) -- Leu(215)	Tyr(114) -- Arg(227)
Phe(109) -- Leu(215)	Asn(115) -- Arg(227)
Ala(110) -- Leu(215)	Thr(116) -- Arg(227)
Ala(111) -- Leu(215)	Thr(103) -- Ser(213)
Ala(112) -- Leu(215)	Glu(104) -- Ser(213)
His(113) -- Leu(215)	Glu(105) -- Ser(213)
Tyr(114) -- Leu(215)	Thr(106) -- Ser(213)
Asn(115) -- Leu(215)	Ile(107) -- Ser(213)
Thr(116) -- Leu(215)	Lys(108) -- Ser(213)
Thr(103) -- Ser(228)	Phe(109) -- Ser(213)
Glu(104) -- Ser(228)	Ala(110) -- Ser(213)
Glu(105) -- Ser(228)	Ala(111) -- Ser(213)

Thr(106) -- Ser(228)

Ile(107) -- Ser(228)

Lys(108) -- Ser(228)

Phe(109) -- Ser(228)

Ala(110) -- Ser(228)

Ala(111) -- Ser(228)

Ala(112) -- Ser(228)

His(113) -- Ser(228)

Thr(106) -- Lys(214)

Ile(107) -- Lys(214)

Lys(108) -- Lys(214)

Phe(109) -- Lys(214)

Ala(110) -- Lys(214)

Glu(105) -- Leu(229)

Thr(106) -- Leu(229)

Ile(107) -- Leu(229)

Lys(108) -- Leu(229)

Phe(109) -- Leu(229)

Ala(110) -- Leu(229)

Ala(111) -- Leu(229)

Ala(112) -- Leu(229)

His(113) -- Leu(229)

Tyr(114) -- Leu(229)

Asn(115) -- Leu(229)

Thr(116) -- Leu(229)

Ala(112) -- Ser(213)

His(113) -- Ser(213)

Tyr(114) -- Ser(213)

Asn(115) -- Ser(213)

Thr(116) -- Ser(213)

Thr(103) -- Lys(214)

Glu(104) -- Lys(214)

Glu(105) -- Lys(214)

Please replace the paragraph on page 24 that begins on line 18 with the following amended paragraph:

Preferred embodiments include the following deletion mutants: Thr(103) -- Arg(227); Glu(104) -- Arg(227); Ala(112) -- Arg(227); Thr(103) -- Ser(213); Glu(104) -- Ser(213); Thr(103) -- Leu(215); Glu(47) -- Ser(419); Met(1), Glu(~~23~~ 24), or Ala(24 25) -- Met(263); Met(1), Glu(~~23~~ 24), or Ala(24 25) -- Asp(311); Met(1), Glu (~~23~~ 24), or Ala(24 25) -- Pro (~~367~~ 366); Met(1) -- Ser(419); and Met(1) -- Ser(228) of (Figure 1 (SEQ ID NO:18)).